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Editorial comment

Analysis of C-reactive protein (CRP) levels in pain patients – Can biomarker studies lead to better understanding of the pathophysiology of pain?

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In this issue of the *Scandinavian Journal of Pain*, Michele Sterling and co-authors present data showing that blood levels of the inflammatory biomarker serum C-reactive protein (CRP) seem to correlate to fMRI responses in regional brain areas, activated by noxious cold stimulation of the hand in patients with chronic whiplash associated disorders (WAD) [1]. The activated brain regions included the anterior insula, posterior parietal cortex, caudate and thalamus. The levels of TNF-alpha were not related to cerebral fMRI changes during pain stimuli, but a moderate positive correlation was found between blood levels of TNF and the psychological variable of pain catastrophizing.

The study shows the interesting possibility to use analysis of biomarkers in blood as a way for deeper understanding of the biological aspect of pain, this elusive "bio-psycho-social" construct, combined with "imaging biomarkers" using fMRI.

I think it is realistic to say that in the parts of the medical community, pain patients and pain treatment often are considered as "low status" work, and difficult to handle. One reason behind this view may be the fact that the golden standard of pain assessment is based upon the patient's self-report only, and that objective, measurable findings usually are absent. Of course, we must trust the patient's report, but I often wish that we had better tools to understand the nature of pain and its pathophysiology.

"We need a CRP for pain", a colleague pain clinician once said, "some lab test that would show that there is something measurable going on in the pain patient. This would improve the respect for the pain patients from the caregivers, and give the field of pain medicine a better status" (personal communication, Jens Draiby, 2014).

It is not realistic to believe that we can measure the actual pain experience through biomarker studies, since pain by definition is a subjective experience that cannot be measured that way. But, perhaps biomarker studies in body fluids (e.g. blood, CSF, saliva, or micro dialysate from painful tissue) can help us to better understand what actually is going on in the pain patients from a pathophysiological point of view? Could some aspects of these complex processes involved be objectively measured using biomarkers? Virtually all other medical specialties have a foundation in analysis of biomarkers for diagnosis of diseases, and as a guide for treatment choice, and treatment effects. Still, biomarker research in pain patients is, by large, "terra incognita", but we would certainly need more of this in our work to help pain patients better.

The cause of elevated CRP levels in patients with chronic WAD is not clear. What is the chain of events, starting with a WAD injury that may lead to increased production of CRP in the liver? It may be as a result of unresolved peripheral tissue damage in cervical spinal structures [2], resulting in a subclinical systemic inflammatory response including release of CRP. The analysis of CRP gives only limited information about on-going inflammatory processes. The use of more sensitive analytic tools for detection of inflammation, recently available, such as multiplex arrays for the multitude of mediators involved in the inflammatory cascade [3], may provide more detailed information on these complex events.

The study design and the methods used by Sterling et al. are advanced – selecting a clinical pain state (WAD), investigating the blood levels of inflammatory markers, and study possible correlations of cold stimuli and brain activation using fMRI in the same patient. Possible connections between levels of inflammatory biomarkers and psychological factors were also looked for, as an interesting attempt to "unite" psychological issues to biology. There are also some limitations of the present study. The number of subjects included in the study is small, including only patients and no controls. The levels of inflammatory biomarkers were not corrected for influences of body mass, which may be of importance.

Nevertheless, the study by Sterling et al. [1] indicates that research on inflammatory biomarkers in pain patients may contribute to a better understanding of the biological aspects of the complex pathophysiology of pain. It is a good early attempt in the search for the "CRP for pain patients".

Conflict of interest

None declared by the author.

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